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EXAMINER	
TON, THAIAN N	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,994	LUYTEN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-59,61 and 62* is/are pending in the application.

4a) Of the above claim(s) *31-42 and 46-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-45,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Amendment and Remarks, filed 4/21/06, has been entered. Claims 31-42 and 46-59 are withdrawn; claims 43, 44 are amended; claim 60 is cancelled; claim 62 is added; claims 43-45, 61 and 62 are under current examination.

Election/Restrictions

Claims 31-42 and 46-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/4/05.

Applicant's election without traverse of Group XII (claims 43-45, 60 and 61) in the reply filed on 8/4/05 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for reasons of record, advanced in the prior Office action, mailed 10/21/05.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments. Applicants state that the Office action, "does not question that the specification enables subject matter to precursor cells expressing the CDMP-1 marker," and that the "rejection is based upon the assertion that (1) the specification fails to provide specific guidance with regard to isolation of cells using any of the markers, other than CDMP-1 in order to arrive at the claimed invention." See page 12, 1st ¶ of the Response. Applicants argue that in order to sustain the rejection, the Examiner must find that a person of skill in the art would not have known that the methods outlined in the specification, in combination with Applicants' description of the positive CDMP-1 marker (and negative markers) and the knowledge of those skilled in the art, would enable the isolation and identification of other positive embryogenic markers. See page 12 of the Response.

Response to Arguments. These arguments are not persuasive. Applicants are misinterpreting the prior rejection of record. The Examiner has not stated that CDMP-1 is enabled for the isolation of the precursor cells. It is noted that if this were the case, then a scope of enablement would present the enabled aspect of the invention. This is not the instant case. In summary, the prior rejection clearly states that the breadth of the claims is now directed to the identification of cells expressing CDMP-1 or markers co-expressed or co-detectable with this marker. The specification does not provide guidance or teachings with regard to the markers that are co-expressed/co-detected with CDMP-1. Furthermore, Luyten *et al.* (**Int. J. Biochem. Cell Bio.**, 29(11): 1241-1244 (1997) teach that CDMP-1 is expressed postnatally in various tissues, including cartilage, brain and placenta (p. 1242, col. 1-2, bridging sentence). Thus, one of skill in the art could not predictably arrive at the claimed cells, because one of skill in the art would not know how to isolate the

cells, as instantly and broadly claimed, by using one known marker (CDMP-1), or using CDMP-1 and an unknown marker. Thus, the Examiner has shown that one of ordinary skill in the art would have had to practice undue experimentation, to arrive at the claimed invention.

Applicants' Arguments. Applicants argue that identifying and characterizing a marker co-expressed/co-detected with CDMP-1 is indeed straightforward. See pages 12-13. Applicants argue that they have characterized not only the CDMP-1 marker, but also several negative markers, including FGFR3. Thus, Applicants argue, because they have defined these markers, there is no undue experimentation involved in ascertaining additional markers within the scope of the present claims. See pages 13-14. Applicants argue that newly added claims 61-62 are directed to a negative marker, and are clearly free of the enablement rejection, because they have demonstrated that FGFR3 is a negative marker, and that markers such as type 11 collagen, type X collagen and BMP2 represent markers that are co-expressed or co-detectable with FGFR3. See pages 16-17.

Response to Arguments. These arguments are considered, but not persuasive. It should be made clear that, the enabling specification must teach those skilled in the art to make and use the full scope of the claimed invention without undue experimentation. "Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." *Vaeck*, 947 F.2d at 495, 20 USPQ2d at 1444; *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404; *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification)." *In re Wright* (CAFC) 27 USPQ2d 1510 at 1513. Applicants are arguing limitations that are not found in the claims. Although Applicants have identified a negative marker, FGFR3, the independent claim does not recite this.

Furthermore, a negative marker is not within the broad scope of the claims, which require a marker that is either expressed or detectable with CDMP-1 (see claims 43-45). A negative marker is not expressed. Claim 61 requires that the cells are characterized by the absence of a negative marker (FGFR3), or a marker or factor co-expressed or co-detectable with FGFR3. It is unclear how this would further characterize the cells, because the negative marker is not expressed, thus how could one identify markers or factors that are co-expressed with an unexpressed marker? The specification provides no guidance or teachings with regard to how to characterize cells using a negative marker (*i.e.*, one that is not expressed) or markers that are expressed in the absence of expression of the negative marker.

Wands. Applicants argue that, having access to their newly disclosed marker (for example, CDMP-1 and FGF3), one of skill in the art could find additional markers from precursor cell lines, absent undue experimentation, simply by following the teachings found in the specification. Applicants point to *In re Wands*, to support that their specification satisfies the first test as outlined by Wands, namely that a considerable amount of experimentation is permissible if it is merely routine. See page 13 of the Response. Applicants argue that, alternatively, applying the second test of *Wands,* a reasonable amount of guidance is provided by their specification. Applicants argue that they have outlined general methods useful for identifying and characterizing additional positive embryogenic markers (Examples 1-3), and also provide methods for testing the phenotypic stability of the cells (Examples 4-5), as well as examining the ability of the cells to form cartilage *in vitro* and *in vivo*. Applicants argue that the teachings of the specification are, in and of themselves, more than adequate to satisfy the requisite "reasonable amount of guidance". Thus, Applicants argue that this general teaching easily places their specification within the bounds set out by *Wands* in its second test for enablement. See page 14, 2nd ¶ of the Response. Applicants argue that the specification's teachings, and disclosed positive embryonic markers, it would be a trivial matter to

identify additional markers from the precursor cells isolated and characterized by Applicants, using the methods outlined by their specification. The experimentation that would be involved would be straightforward and routine. Applicants argue that the specification adequately describes the methods used to practice the claimed invention, and that there is no evidence currently made of record that establishes a basis for doubting the objective truth of the statements found in the specification, with regard to "a marker co-expressed and/or co-detectable with CDMP-1". See pages 15-16, bridging ¶.

Wands. Applicant correctly asserts that a large amount of experimentation is acceptable, if that experimentation is merely routine. However, the amount of experimentation required to make and use the full scope of the claimed invention, as evidenced by the prior Office actions, is more than simply routine. Applicants have only taught expression of CDMP-1 as a marker for use in identification of the claimed cells. Because CDMP-1 is expressed in various tissues, one of skill could not use this marker to uniquely identify the claimed cell populations. The other markers that are contemplated (those which are co-expressed or co-detected with CDMP-1) are not specifically taught, and one skilled in the art could not use the guidance provided by the specification to identify the cell populations. One of skill would need to practice undue experimentation to first identify these unknown markers and then determine if the marker(s) were expressed solely in the claimed cell types, or in other cell types, in order to uniquely identify the claimed cell population. In *Wands*, the invention was limited to a single class of antibody capable of detecting a single antigen, as opposed to the broad scope of identifying the cells, as claimed, by a marker that is expressed in various cell types, or using an unidentified marker to identify the pluripotent precursor cells that have entered a postnatal skeletal differentiation pathway leading to skeletal or connective tissue. The Court in *Wands* reasoned as follows (1406-1407; emphasis added):

> When Wands' data is interpreted in a reasonable manner, analysis considering the factors enumerated in *Ex parte Forman* leads to the

> conclusion that undue experimentation would not be required to practice the invention. Wands' disclosure provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known. The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which ones secrete antibody with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. No evidence was presented by either party on how many hybridomas would be viewed by those in the art as requiring undue experimentation to screen. However, it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened. Furthermore, in the monoclonal antibody art it appears that an "experiment" is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen. This process entails immunizing animals, fusing lymphocytes from the immunized animals with myeloma cells to make hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristics. Wands carried out this entire procedure three times, and was successful each time in making at least one antibody that satisfied all of the claim limitations. Reasonably interpreted, Wands' record indicates that, in the production of high-affinity IgM antibodies against HBsAG, the amount of effort needed to obtain such antibodies is not excessive. Wands' evidence thus effectively rebuts the examiner's challenge to the enablement of their disclosure.

In contrast to the facts in *Wands*, the instant claims are tremendously broad, because they provide only a single marker (or a combination of CDMP-1 with unidentified marker(s)) that would be used to identify the precursor cells. Aside from CDMP-1, the specification provides no specific guidance with regard to how to identify the claimed precursor cells. Thus, it is maintained that it would have required undue experimentation to practice the claimed invention.

Therapeutic Benefit. Applicants argue that human testing is not required for enablement purposes, to support claims of an *in vivo* utility of a biomedical invention. Applicants argue that the law is very clear, in that enablement requires

nothing more than objective enablement and in a case where the Patent Office questions the enablement of a claim, evidence from sources other than human efficacy trials is acceptable. See page 17 of the Response. Applicants argue that they meet this standard, because they show the formation of chondrocytes with skeletal precursors both *in vivo* and *in vitro*. Applicants argue that because the human skeletal precursor cells were administered with pig articular chondrocytes that resulted in cartilage forming potential of the chondrocytic cells, this demonstrates that the claimed method would be successful, and enables the invention. Applicants argue that there is no evidence that injection of cells that are not autologous to the individual would fail to integrate or function, because models of the sort have been described in the specification. Applicants argue that the reliance on Hui is inappropriate because Applicants, in fact, identified several markers useful in identifying skeletal precursors, a goal that Hui proclaims as desirable. Applicants argue that the concerns regarding autologous cell transplantation are unwarranted, because the specification teaches that this is becoming a widely accepted technique for repair of joint surface defects. See page 18 of the Response.

Response to Arguments. These arguments are considered, but not persuasive. The intended use of the claimed therapeutic compositions/implants is for purposes of therapy. Although human testing is not required for enablement, the claims must be enabled for both making and use. In the instant case, the cells, as claimed by Applicants, fail to be enabled for the reasons stated above, namely, that the markers claimed would fail to provide a unique cell population. Given that one of skill in the art would not be able to specifically isolate the cells, it would be unpredictable that one could use these unknown cell populations for methods of therapy. Hui *et al.* do discuss that various markers would be useful in identifying particular cell types that would be used in methods of musculoskeletal tissue engineering. Although Applicants have postulated using various markers that

might be used in these methods, as stated above, they have not enabled using these markers (such as those co-expressed or co-detectable with CDMP-1 or FGFR3) to isolate a particular cell type, which could be used in the contemplated therapeutic methods. Thus, Hui *et al.* clearly show that even post-filing, it would not be predictable to isolate a particular cell type with unknown/undisclosed markers, to engineer tissues. Neither Applicants' arguments, nor the art of record support that one could predictably isolate the claimed cells, and use them in methods of implantation for producing tissues, without undue experimentation. One of skill in the art would need to practice undue experimentation in order to isolate the cells, and then practice undue experimentation to use these cells in methods of therapy. It is reiterated that the working examples fail to correlate to a therapeutic result in utilizing the claimed cells, as they are directed to injection of immunodeficient, nude mice, which would not be considered a model for an immunocompetent individual. The working example shows *in vivo* implantation of the cells by intramuscular injection of the cells into nude mice. This is not analogous to what would be considered a therapeutic treatment. For example, the specification contemplates the instant invention in the context of a mammal with cartilage defects (see page 22, lines 23-35, for example). The nude mouse, as taught in the working example, is not considered a model of cartilage defect. Although the specification teaches that an increase in chondrocytes, this does not provide a nexus to show implantation of the instantly-claimed cells, in an appropriate model which would result in connective tissue repair, or would differentiate into cells that would integrate and function to repair the damaged or malfunctioning tissue. One of skill in the art could not rely upon the state of the art to provide this nexus, as stated in the prior Office action, because implantation of stem cells, and particularly cells that form chondrocytes or osteoblasts, that function in a physiologically appropriate manner to provide therapy, is found to be unpredictable. See pages 5-6 of the prior Office action.

The Amount of Experimentation Necessary. Accordingly, it is maintained that the specification fails to provide specific teachings or guidance the claimed embodiments of isolated skeletal precursor cells, because the methods taught by the specification only provide a particular marker, CDMP-1, to identify these cells. However, beyond using this single marker, the specification provides no other defining characteristics of the resultant cells. Although the working examples provide guidance with regard to the production of cartilage from the cells, upon administration of TGF-β, this fails to provide guidance with regard to the actual cells that are isolated. In view of the lack of teachings or guidance, with specific regard to the identification of the skeletal precursor stem cells, except by the identification of a particular marker (CDMP-1), the unpredictability in the art with regard to the intended use of the therapeutic compositions/implants for therapeutic purposes, the lack of teachings or guidance with regard to define the cells used in the working examples, the lack of nexus between the *in vivo* example, utilizing a nude, immunodeficient mouse and any resultant therapeutic effect, it would have required undue experimentation for one of skill in the art to practice the claimed invention.

Written Description

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for reasons of record advanced in the prior Office action, mailed 10/21/05.

Applicants' Arguments. Applicants argue that written description does not require application to describe exactly the subject matter claimed, but must allow

for persons of ordinary skill to recognize that he/she invented what is claimed. Thus, Applicants argue that their application teaches one of ordinary skill to produce the culture of isolated and expanded viable, differentiated, pluripotent precursor cells that have entered a post-natal skeletal differentiation pathway. Applicants argue that that cells express a positive marker, CDMP-1. Applicants point to various parts of the specification, with regard to support for the claimed invention. See pages 19-21 of the Response.

Response to Arguments. Although Applicants have literal support for the various embodiments that they claim, they fail to meet the written description requirement, because the claims require essential or critical elements which are not adequately described in the specification. For example, claim 43 recites using CDMP-1, or a marker co-expressed or co-detectable with CDMP-1. As stated in the enablement rejection, above, CDMP-1 is expressed in various tissues, such as brain, placenta and cartilage. Although one might expect the claimed cells to be present in cartilage, one would not expect these cells to be present, in brain, for example. Thus, utilizing only CDMP-1 as a marker for identification of the cells may not provide the cell population, as claimed. Claim 43 alternatively claims that the cells could express a marker that is co-expressed or co-detectable with CDMP-1. These markers are not described by the specification because the specification fails to describe what markers and the resultant cells would belong to this genus. Similarly, claim 61 recites that the cells can additionally be characterized by the absence of a negative marker, FGFR3, or a marker or factor co-expressed or co-detectable with FGFR3. These markers are not described by the specification, because there is no guidance, for example, with regard to how one would identify markers that are co-expressed with a marker that is not expressed. Simply put, if a marker is not expressed, those markers that are co-detectable with it would not be able to be identified.

Furthermore, the claims lack written description with regard to "cells that have entered a post-natal differentiation pathway leading to skeletal or connective tissue." The specification fails to provide any guidance as to how to identify precursor cells that have entered a postnatal differentiation pathway, versus those that have not entered the pathway. The specification fails to provide guidance, even using CDMP-1, with regard to how one would discern between cells that have entered the pathway from cells that have not. Absent a particular marker, phenotype or any other specific identifying factor, one could not distinguish between the cells that have entered the pathway from those which have not. Thus, the claimed cells, which have entered a post-natal differentiation pathway, lack written description.

Although the specification teaches that the cells of the instant invention are characterized in that they express CDMP-1, there is no specific characterization of the cells to indicate that they are differentiated pluripotent precursor cells that have entered the post-natal skeletal differentiation pathway. The skilled artisan could not envision which of the markers, encompassed by the claims, would be expressed, or not expressed, in the cell population instantly claimed, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Accordingly, it is maintained that the claimed invention lacks written description.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is

maintained for reasons of record, advanced in the prior Office action mailed 10/21/05.

The metes and bounds of the claims cannot be ascertained for the following reasons: claim 43 recites a "differentiated, pluripotent precursor cell". Claims 44, 45, 61 and 62 depend from claim 43.

Applicants' arguments. Applicants' argue that the specification teaches that the instantly-claimed cell is already committed towards the differentiation pathways of the skeletal tissues, but is still pluripotent and may differentiate into any of the connective tissues or a subgroup thereof.

Response to Arguments. It is unclear how a cell can be differentiated and pluripotent simultaneously. Applicants are directed to the glossary provided by the NRC (Guidelines for Human Embryonic Stem Cell Research, Natl. Academies Press, Washington DC, 2005, pages 116 and 119). Page 116 provides the definition for differentiation as, "The process whereby an unspecialized early embryonic cell acquires the features of a specialized cell, such as a heart, liver or muscle cell." Page 119 provides the definition of a pluripotent cell as, "A cell that has the capability of developing into cells of all germ layers (endoderm, ectoderm, and mesoderm)." (*Emphasis added*). Applicants' arguments are not persuasive because a pluripotent cell, as claimed here, is one that can develop into all three germ layers. Applicants' cells are not capable of this – as clearly noted by the cited passage, which shows that it can only differentiate into pathways that form cells of skeletal tissues or connective tissue. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "pluripotent" is used by the claim to mean "cells that can differentiate into

pathways of form cells of skeletal tissues or connective tissue", while the accepted meaning is "cells that can differentiate into all three germ layers." The term is indefinite because the specification does not clearly redefine the term.

The prior rejection of claim 43, with regard to the term "a marker co-expressed and/or co-detected with this marker" is withdrawn.

Claim Rejections - 35 USC § 102

The prior rejection of claims 43-45, and 60 under 35 U.S.C. 102(b) as being anticipated by Connolly is withdrawn because Applicants have now amended the claims to recite that the cells express either CDMP-1, or a marker co-expressed or co-detectable with CDMP-1, which is not taught by Connolly.

New rejections to the claims appear below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 43-44, 61 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Takahashi *et al.* (**J. Clin. Invest.**, 83: 543-550 (February 1989)).

The claims are directed to a culture of isolated and expanded viable, differentiated pluripotent precursor cells that have entered a post-natal skeletal differentiation pathway leading to skeletal or connective tissue, wherein the cells express a positive embryonic marker, which is CDMP-1, or a marker co-expressed and/or co-detectable with CDMP-1. Further embodiments are directed to a therapeutic composition comprising said culture, an implant comprising the cells.

Takahashi *et al.* teach isolation of bone marrow aspirates from human donors (see p. 543, 1st col., last ¶).

The claims are interpreted as follows: the culture of isolated and expanded viable, differentiated pluripotent precursor cells (claim 43) are taught in the specification to be isolated from various sources, including bone marrow (see page 24, lines 4-7 and Examples 1 and 3). Because the culture, as taught by Takahashi, is also isolated from bone marrow, it would reasonably contain the instantly claimed cells. Because the cells of Takahashi and the cells that are instantly claimed are from the same source (bone marrow), they would necessarily (inherently) express the markers that are required by the claims (CDMP-1, markers co-expressed and/or co-detectable with CDMP-1), and the absence of expression of FGFR3.

"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke.

Furthermore, the phrase "a therapeutic composition" (claims 44, 64) merely sets forth an intended use of the claimed composition and does not serve to further define the compositions. *In re Pearson,* 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974), citing *Kropa v. Robie*, 187 F.2d 150, 88 USPQ 478 (CCPA 1951); *In re Lemin*, 326 F.2d 437, 140 USPQ 273 (CCPA 1964), and *In re Zierden*, 411 F.2d 1325, 162 USPQ 102 (CCPA 1969).

Accordingly, Takahashi *et al.* anticipate the claimed invention.

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlacher *et al.* (**Arthritis & Rheumatism**, 41(2): 263-273 (February 1998).

Erlacher *et al.* teach the isolation of adult bovine and human articular cartilage, culturing of the cartilage of the cells. They found that both bovine and human articular cartilage expressed CDMP-1. See Abstract, p. 264, 2nd column, Source of human articular cartilage. They teach that the articular cartilage was then cultured in medium, and then and maintained as a cartilage explant (p. 264, 2nd col.Cartilage Explant Cultures). Thus, Erlacher *et al.* teach cells that express CDMP-1, which, according to the claims, characterize the precursor cells. The terms "therapeutic composition" and "implant" define an intended use for the cells, which do not impart patentable weight because they do not serve to further define the composition. Because Erlacher *et al.* teach cells that express CDMP-1, these cells would inherently have the characteristics required by the claims, such as being differentiated, pluripotent precursor cells that have entered a post-natal skeletal differentiation pathway leading to skeletal or connective tissue.

Accordingly, Erlacher *et al.* anticipate the claims.

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang *et al.* (JBC, 269(45): 28227-28234 (Nov. 11, 1994, cited in the prior Office action).

Chang *et al.* teach partially purified extracts from newborn calf articular cartilage that induced cartilage and bone when subcutaneously implanted into rats. They found that the extracts expressed CDMP-1 (see Abstract). As with the rejection above, because Chang *et al.* teach cells that express CDMP-1, these cells would inherently have the characteristics required by the claims.

Accordingly, Chang *et al.* anticipate the claims, because they teach a culture that expresses CDMP-1 and was used as an implant, which is required by the claims.

Claims 43-45, 61 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Kyoizumi *et al.* (**Blood**, 79(9): 1704-1711 (April 1, 1992).

Kyoizumi *et al.* teach fetal tibia were obtained from cultured human fetal tissues, and implanted subcutaneously in SCID mice (see p. 1704, 2nd column).

Because Kyoizumi *et al.* teach isolation of cells from the same source (human tibia, see p. 23, Example 1, lines 23-25), their culture would necessarily contain the claimed cells, and those cells would necessarily express the markers required by the claims.

Accordingly, Kyoizumi *et al.* anticipate the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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